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TI Analysis of antigen presentation by metabolically inactive accessory cells and their isolated membranes
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AB Several amino acid copolymers are potent immunogens under the control of major **histocompatibility** complex (MHC)-encoded Ir genes. Their accessory-cell-dependent, MHC-restricted presentation to T lymphocytes was characterized. Their processing requirements were initially characterized by investigating the ability of paraformaldehyde-fixed antigen-presenting cells (APC) to present these copolymers. Fixed APC can present poly(Glu56Lys35Phe9) and poly(Glu60Ala30Tyr10) provided that they have been incubated with antigen prior to fixation. The inability of these same fixed prepns. to present sol. antigen indicates a fixation-sensitive antigen-processing step. In contrast, the antigens poly(Glu55Lys35Leu10) and poly(Glu55Lys35Tyr10) can be presented by APC fixed before antigen exposure. This differential requirement for antigen processing was exploited to analyze the events of antigen presentation in 2 related systems. First, the ability of isolated APC membranes to process and present antigen was assessed. APC membranes can present the antigens poly(GluLysLeu) and poly(GluLysTyr) in a specific and MHC-restricted manner. However, the isolated membranes fail to present either poly(GluLysPhe) or poly(GluAlaTyr), suggesting that such prepns. can present but not process antigen. Second, the distinct properties of the various copolymers were used with fixed APC to test the effects of antigen processing on the phenomenon of antigen competition. APC that had processed poly(GluLysPhe) or poly(GluAlaTyr) were subsequently fixed and used to present antigen in the presence or absence of various antagonists. Under these conditions, poly(GluLysLeu) and poly(Glu50Tyr50) could effect specific inhibition, clearly indicating that antigen competition occurs distal to and does not require antigen processing. In contrast, native antigen with an abs. processing requirement is not capable of competing with preprocessed antigen on fixed APC. Apparently, processing is important for the mol. interactions between the copolymer antigens and the APC cell surface that are relevant to both antigen presentation and competitive inhibition.